

REMARKS

AMENDMENTS

IN THE CLAIMS

Applicants present amendments to claims 12 and 22 which effect changes requested by the examiner. In addition, applicants introduce new claims 24-27, and respectfully request that they be entered. These claims are limited to the present process wherein the new catalytic activity is within that IUB class already assigned to the original enzyme. Support for this new limitation is found in the specification at page 4, line 10, which introduces the IUB classification system, and from the example beginning on p.11, in which the new catalytic activity is within the IUB class assigned to the enzyme originally.

IN THE SPECIFICATION

Applicants again amend Table I on page 10 of the specification. This amendment is to introduce and/or clarify the proper trade names for the products referred to therein upon filing. Support for the amendment comes from the inherency of these names, as further set forward below. Additionally, portions of the specification previously amended have been amended again to more clearly indicate applicants' intent.

OBJECTIONS TO THE SPECIFICATION

PARENTHETICAL STRUCTURE

In amending the parenthetical structure objected to, applicants intended that the equals sign, "=", be removed. Consistent with current amendment requirements, this sign has been struck through, like so "=". Accordingly, it should not have been retained. In each instance of the noted parenthetical structure, applicants have attempted to replace the "=" with "i.e.," or some similar term, or have simply let the parentheses serve their common grammatical function(s). It is respectfully submitted that the present amendments clarify this situation.

REDUCTION OF K_m /INCREASE OF k_{cat}

It is respectfully submitted that a reference value for K_m and/or k_{cat} is unnecessary for present purposes. In the present invention, the relative change is to be observed qualitatively, and the numerical value of the change is not important. Whether such change is due specifically to a reduction in K_m or an increase in k_{cat} , and to what precise extent it is due to either, is of little to no import.

TRADE NAMES OF ENZYMES

The amendments to Table I on page 10 of the specification introduced the trade names of the commercially available enzymes employed in the examples beginning on page 9. Attached hereto are printed pages from various sources which indicate that the terms Amano, Lipoxyme, and Novozyme (amended herein to "Novozym," which is

technically more correct) would be inherently observed by one of skill in the art when reading the information in the table as originally filed.

Applicants attach pages from the Amano Enzyme, Inc. website, which list the following products: Lipase PS “Amano,” Lipase AH “Amano,” Acylase “Amano,” Lipase D “Amano,” Lipase F-AP 15, Lipase AY “Amano,” Lipase M “Amano” 10, Lipase R “Amano,” and Lipase G “Amano” 50. Pages taken from the Sanger Institute website and from the German Collection of Microorganisms and Cell Cultures (DSMZ) website, also attached, indicate the equivalence between *Burkholderia cenocepacia* and *Pseudomonas cepacia*, and *Rhizopus oryzae* and strains *R. javanicus* and *R. delamar*, respectively.

Pages printed from the Novozymes A/S website indicate use of the words “Novozym” and “Lipozyme” for commercially available products manufactured by that company. The attached abstract of Yamamoto, et al. recites use of “two lipases[:] Amano PS (*Pseudomonas* sp.) and Novozym 435[®],” indicating recognized use of these terms by skilled artisans. Likewise, the attached paper by Maugard and Legroy indicates that “Novozym[®] SP 435 (lipase from *Candida antarctica* immobilised on an acrylic resin), [and] Lipozyme[®] (lipase from *Rhizomucor miehei* immobilised on an anionic macroporous resin ...), were [obtained] from Novo Industries (Denmark).” Novo has since moved its industrial enzyme production to Novozymes A/S (see printed page from Novozymes referencing the Demerger Document).

Applicants respectfully submit that from these documents, as well as from a quick search of the relevant literature, the examiner may conclude that the introduced

trade names are not new matter. To one of skill in the art, familiar with the commercially available enzymes, these additional terms would be inherently present in the table as originally filed.

Likewise, the supplied literature amply supports identification of the relevant enzymes as lipases.

REJECTIONS UNDER 35 USC §112, ¶2

FUNCTIONAL EQUIVALENTS

The entire context in which *E. coli* XL1 Red is discussed in the specification indicates that the relevant function of this strain is mutation. The necessary genetic markers mutS, mutT, and mutD5, now recited in the claims, each create deficiencies in the *E. coli* DNA replication process. Applicants feel that the specification provides ample indication of the relevant functional equivalence for purposes of the presently claimed process. However, to assuage whatever residual uncertainty remains in the examiner's mind, applicants have indicated this function by appropriate amendment.

ABBREVIATIONS PS AND AH

As indicated above, Lipase PS and Lipase AH are art-recognized portions of trade names under which certain lipases from *Pseudomonas candida* are sold by Amano Enzyme, Inc. The name "Amano" is trademarked in the United States, and as such, should not be used in the claims. The letters PS and AH serve to indicate particular lipase preparations known in the art. From this, and from the above

discussion of the relevant literature, what is meant by “*Pseudomonas cepacia* lipase PS” and “*Pseudomonas cepacia* lipase AH” would be abundantly clear to the skilled artisan.

REL A1

Attached to this amendment are copies of an abstract from S. Metzger, et al., (Characterization of the relA1 mutation and a comparison of relA1 with new relA null alleles in *Escherichia coli*, *J. Biol. Chem.*, 264(35):21146-52 (1989)) and an excerpt from a paper by M. K. B. Berlyn (Linkage Map of *Escherichia coli* K-12, Edition 10: The Traditional Map, *Microbiol. and Mol. Bio. Rev.*, 62(3):814-984 (1998), excerpted pages are 814-822, 834, 856, 866, 885, 888-9, 913, and 948). These documents indicate the level of knowledge held or available to one of skill in the art with reference to the relA1 mutation.

IMPEDING ENZYME ACTIVITY

Applicants have amended the claims to indicate that “a” new catalytic activity is to be introduced into the enzyme, thus making the inherent directionality express. It is respectfully submitted that one of skill in the art would recognize the need or desirability for identifying a specific catalytic activity prior to undertaking the presently claimed process. Once such an inherently necessary step has been performed, both the enzymatic activity which would impede detection and the proper substrate would also be identified.

No limitation is made in claims 12-23 as to the identity of the new catalytic activity to be obtained, or to its relation to the enzyme's original catalytic activity. The new catalytic activity to be obtained may very well be in addition to or in place of that catalytic activity possessed by the identified enzyme prior to performance of the process. The original activity may be maintained, but need not be, necessarily. Such questions would be answerable to one of skill in the art upon performing the particular iteration of the claimed process.

REJECTIONS UNDER 35 USC §112, ¶1

WRITTEN DESCRIPTION - FUNCTIONAL EQUIVALENTS

The examiner states that a "representative number" of species is required to adequately describe the full scope of functional equivalents. However, "possession" of the invention need not be shown by any actual reduction to practice (see, e.g., *Lockwood v. American Airlines, Inc.*, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997)). Rather, a compound must be defined by "whatever characteristics sufficiently distinguish it" (*Amgen, Inc. v. Chugai Pharmaceutical*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991)). There is no absolute requirement for description of an actual reduction to practice, so long as one of skill in the art would recognize that the disclosed element is obvious as disclosed, or may immediately envisage the element, relying on knowledge and level of skill in the art (see, e.g., *In re Deuel*, 34 USPQ2d 1210 (Fed. Cir. 1995); *Fujikawa v. Wattanasin*, 39 USPQ2d 1895 (Fed. Cir. 1996); *In re Ruschig*, 154 USPQ 118 (CCPA 1967)).

In the present case, the specification and claims indicate that functional equivalents of the present mutator strain are derivatives of *Escherichia coli* XL1 Red which possess the gene markers *relA1*, *mutS*, *mutT* and *mutD5*. Production of such derivatives of *E. coli* XL1 Red, given the knowledge and level of skill in the art, would be obvious and straightforward to one of ordinary skill therein. It is respectfully submitted that the present disclosure, coupled with the extensive resources available to the practitioner of genetic recombination, are sufficient to support the claimed range of functional derivatives for purposes of the written description requirement.

ENABLEMENT

Applicants reiterate their belief that the nature of the experimentation required for claims 12-23, though potentially arduous and substantial, would be a matter of routine for the skilled artisan. One of skill in the art would recognize how divergent from an enzyme's original substrate a particular substrate may be to ensure that the new catalytic activity can be produced in that enzyme. The field of enzymology is not so unpredictable that one of skill in the art would not be unable to understand the necessary parameters inherent in practicing the present invention. To answer the examiner's questions, one of skill in the art would apply the knowledge and understanding commonly held with regard to the individual enzyme to be mutated and/or substrate targeted.

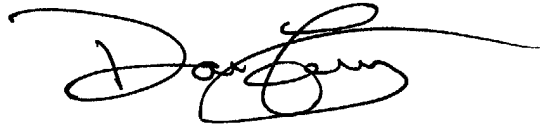
CONCLUSION

In view of the foregoing amendments and remarks, applicants consider that the rejections of record have been obviated and respectfully solicit passage of the application to issue.

Should the examiner disagree, applicants would sincerely appreciate suggestions as to language and/or subject matter which would be considered acceptable.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees to Deposit Account No. 11-0345. Please credit any excess fees to such deposit account.

Respectfully submitted,
KEIL & WEINKAUF

A handwritten signature in black ink, appearing to read 'David C. Liechty', with a long horizontal flourish extending to the right.

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